

**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

**LISTING OF CLAIMS:**

1-10. (Cancelled)

11. (Original) A method for treating cartilage-related disease, which comprises administering a substance having an EP2 and/or EP3 agonist activity.

12-19. (Cancelled)

20. (New) The method according to claim 11, wherein the cartilage-related disease is cartilage disorder.

21. (New) The method according to claim 11, wherein the substance having an EP2 and/or EP3 agonist activity has one or more effects selected from stimulating chondrogenesis, stimulating chondrocyte growth, stimulating chondrocyte differentiation, inhibiting cartilage calcification and inhibiting cartilage degradation.

22. (New) The method according to claim 11, wherein the substance having an EP2 and/or EP3 agonist activity has one or more effects selected from stimulating integrin mRNA expression, stimulating fibronectin mRNA expression, stimulating cyclin D1 mRNA expression and inhibiting osteopontin mRNA expression.

23. (New) The method according to claim 21, wherein the one or more effects selected from stimulating chondrogenesis, stimulating chondrocyte growth, stimulating chondrocyte differentiation, inhibiting cartilage calcification and inhibiting cartilage degradation is/are based on one or more effects selected from stimulating integrin mRNA expression,

stimulating fibronectin mRNA expression, stimulating cyclin D1 mRNA expression and inhibiting osteopontin mRNA expression on a chondrocyte or a cartilage tissue.

24. (New) The method according to claim 23, wherein the effect of stimulating chondrocyte growth is based on stimulating cyclin D1 mRNA expression.

25. (New) The method according to claim 23, wherein the effect of inhibiting cartilage calcification is based on inhibiting osteopontin mRNA expression.

26. (New) The method according to claim 11, wherein the substance having an EP2 and/or EP3 agonist activity is administered in combination with one or more substances selected from transforming growth factor- $\beta$ , insulin-like growth factor, basic fibroblast growth factor, epidermal growth factor, growth hormone and platelet-derived growth factor.

27. (New) The method according to claim 11, wherein the substance having an EP2 agonist activity is one or more compounds selected from a compound described in EP860430, a compound described in WO99/33794, a compound described in EP974580, a compound described in WO2003/74483, a compound described in WO95/19964, a compound described in WO98/28264, a compound described in WO99/19300, a compound described in EP0911321, a compound described in US4,132,738 and a compound described in US3,965,143.

28. (New) The method according to claim 27, wherein the compound is one or more compounds selected from

(1) (5Z,9 $\beta$ ,11 $\alpha$ ,13E)-17,17-propano-11,16-dihydroxy-9-chloro-20-norprosta-5,13-dienoic acid,

(2) (5Z,9 $\beta$ ,11 $\alpha$ ,13E)-17,17-propano-11,16-dihydroxy-9-chloroprosta-5,13,19-trienoic acid,

Preliminary Amendment  
National Stage Entry of PCT/JP04/010890

- (3) trans-2-(4-(1-hydroxyhexyl)phenyl)-5-oxocyclopentaneheptanoic acid,
- (4) 2-[3-(4-tert-butylbenzyl)-N-(pyridin-3-ylsulfonyl)amino-methyl]phenoxy]acetic acid,
- (5) [1R[1 $\alpha$ ,2 $\beta$ (1E,4R\*),3 $\alpha$ ]]-3-hydroxy-2-[4-hydroxy-4-(1-propylcyclobutyl)-1-butenyl]-5-oxocyclopentane-heptanoic acid methyl ester,
- (6) (2R,3R,4R)-4-hydroxy-2-(7-hydroxyheptyl)-3-[(E)-(4RS)-(4-hydroxy-4-methyl-1-octenyl)]cyclopentanone, and
- (7) (+/-)-15-deoxy-16- $\alpha,\beta$ -hydroxy-16-methyl PGE1 methylester.

29. (New) The method according to claim 11, wherein the substance having an EP3 agonist activity is one or more compounds selected from a compound described in WO98/34916, a compound described in JP-A-8-239356, a compound described in US4,692,464, a compound described in JP-A-61-249951, a compound described in US4,863,961 and a compound described in US3,985,791.

30. (New) The method according to claim 29, wherein the compound is one or more compounds selected from

- (1) 11 $\alpha$ ,15 $\alpha$ -dimethoxy-9-oxoprostano-5Z,13E-dienoic acid,
- (2) 2-[5-[2-[N-(diphenylmethyl)carbamoyl]ethyl]naphthalen-1-yloxy]acetic acid,
- (3) (1S,5S,6R,7R)-5-[7-hydroxy-6-[3(S)-hydroxy-3-methyl-1(E)-octenyl]bicyclo[3.3.0]oct-2-ene-3-yl]pentanoic acid,
- (4) (-)-[1(R)-[1 $\alpha$ (Z),2 $\beta$ (R\*),3 $\alpha$ ]]-7-[3-hydroxy-2-(2-hydroxy-3-phenylpropoxy)-5-oxocyclopentyl]-4-heptenoic acid 4-(benzoylamino)phenylester,

(5) methyl-7-(2 $\beta$ -(6-(1-cyclopentyl-yl)-4R-hydroxy-4-methyl-1E,5E-hexadienyl)-3 $\alpha$ -hydroxy-5-oxo-1R,1 $\alpha$ -cyclopentyl)-4Z-heptenoic acid, and

(6) 9-oxo-11 $\alpha$ ,15 $\alpha$ -dihydroxy-16-phenoxy-17,18,19,20-tetranorprosta-4,5,13-trans-trienoic acid methyl ester.

31. (New) The method according to claim 11, wherein the compound having an EP3 agonist activity is 16-phenoxy- $\omega$ -17,18,19,20-tetranor-PGE<sub>2</sub> methylsulfonamide or a salt thereof.

32. (New) An agent for treating cartilage-related disease comprising a combination of one or more substances selected from transforming growth factor- $\beta$ , insulin-like growth factor, basic fibroblast growth factor, epidermal growth factor, growth hormone and platelet-derived growth factor, and a substance having an EP2 and/or EP3 agonist activity.

33. (New) A method for producing a cartilage graft, which comprises using a substance having an EP2 and/or EP3 agonist activity.

34. (New) A method for screening an agent for treating cartilage-related disease comprising a substance having an EP2 and/or EP3 agonist activity, which comprises correlating the EP2 and/or EP3 agonist activity.